REMARKS

Applicants wish to thank Examiner Allen for the courtesy extended to their representative, Nancy W. Vensko, on January 22, 2001, in U.S. Pat. Appl. No. 08/428,242, filed Sept 18, 1995. The Interview Summary Form PTOL-413 summarizes the discussions held at the personal interview (attached). The present remarks address the substance of the Examiner Interview.

I. Disposition Of Claims

Claims 1-16 are presented for examination.

II. Human and Rat Serotonin Receptor Protein St-B17

The invention relates to isolated human serotonin receptor protein St-B17 (Claim 1) and isolated rat serotonin receptor protein St-B17 (Claim 9), and related constructs, polynucleotides, cell lines, and products-by-process.

III. No New Sequence Listing

While disagreeing with the position by the PTO that depositing a biological material after the priority date introduces new matter into this application, to advance prosecution Applicant has refrained from introducing a biological deposit or deposit information herein. Neither has Applicant introduced a new sequence listing in paper form or computer readable form (CRF) into this application to conform to any biological deposit. Rather, Applicant has copied the *original* sequence listing in paper form and computer readable form (CRF) that was filed in response to the Notice to Comply in the parent application to which this continuation application relates back.

IV. Corrected Rat and Human Sequences

Under 37 CFR 1.56, Applicant wishes to meet his duty to disclose by making of record errors in the sequence listing.

Beginning with rat, SEQ ID NO:7 is the DNA sequence and SEQ ID NO:8 is the amino acid sequence encoding rat serotonin receptor protein St-B17, as originally filed on October 26, 1992. The inventors and their colleagues subsequently published this

sequence as Monsma et al., Molecular Pharmacology 43:320 (March 1993) (attached). Other colleagues published this sequence as Ruat et al., Biochem Biophys Res Comm 193:268 (May 1993) (attached). Later, the inventors and their colleagues published the corrected sequence in Kohen et al., J. of Neurochemistry 66:47 (1996) (attached), which points out the particular changes in both the DNA and amino acid sequences.

Turning to human, SEQ ID NO:12 is the DNA sequence and SEQ ID NO:13 is the amino acid sequence encoding human serotonin receptor protein St-B17, as originally filed on October 26, 1993. The inventors and colleagues subsequently published the corrected sequence in Kohen et al., supra. Exhibit 1 (attached) points out the particular changes in the DNA sequence, and Exhibit 2 (attached) points out the particular changes in the amino acid sequence.

V. Claiming by Crucial Third and Sixth Transmembrane Domains

The claims are directed to isolated human serotonin receptor protein St-B17 (Claim 1) and isolated rat serotonin receptor protein St-B17 (Claim 9), and related constructs, polynucleotides, cell lines, and products-by-process, where the serotonin receptor protein St-B17 is defined by reference to crucial transmembrane domains III and VI. Trends in Pharmacology 13:160 (April 1992) (attached) shows that, at the time of the Oct 26, 1992 priority date of the present application, most serotonin receptors were known to be G protein-linked receptors having a putative seven transmembrane domain structure. Here is Trends in Pharmacology Figure 3 showing putative transmembrane domains numbered I to VII for previously known serotonin receptors:

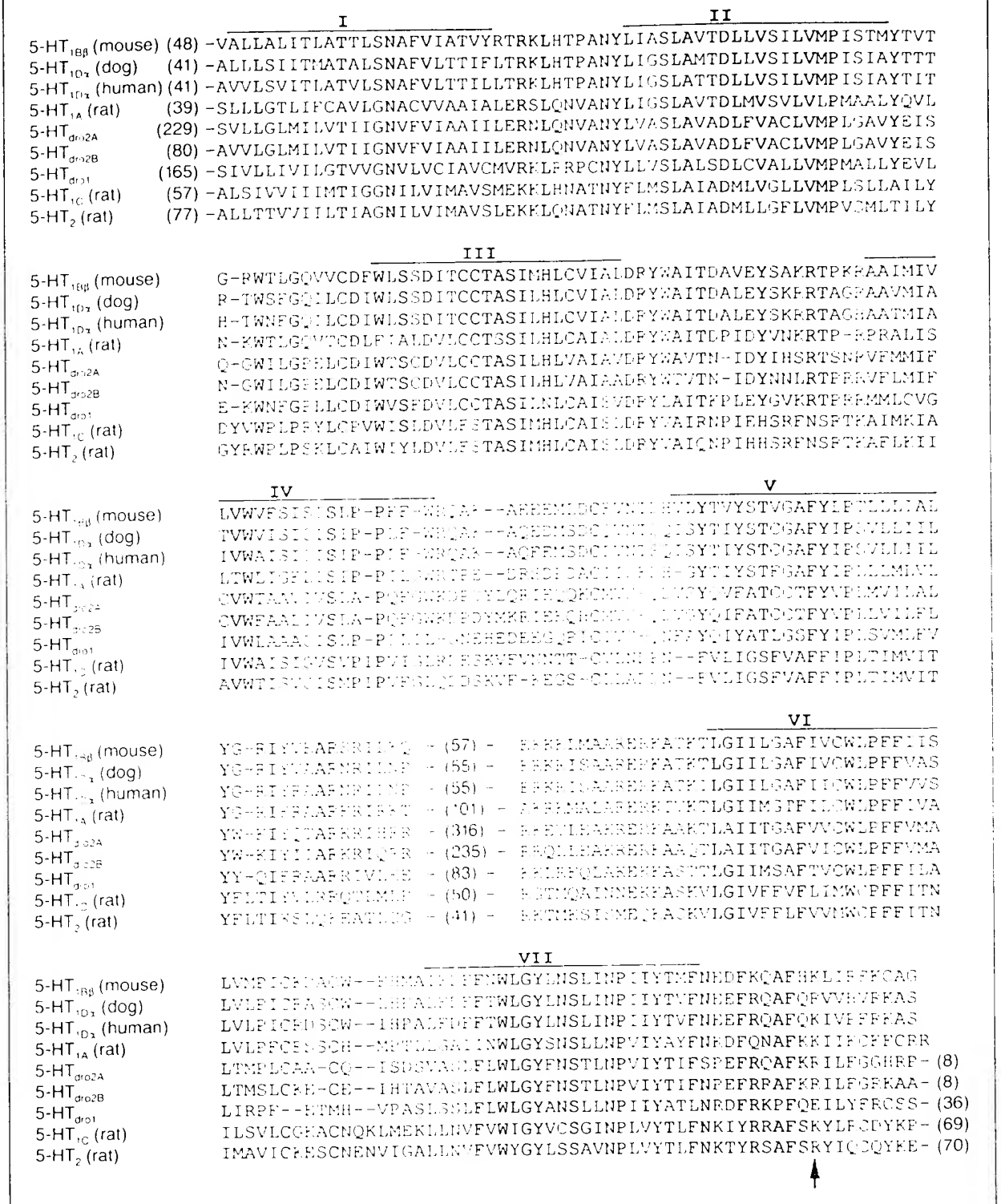


*Fig. 3. Aligned amino acid sequence homologies of 5-HT receptors.* **Tint** *shows positions where more than 6 out of the 9 sequences are identical. Putative transmembrane domains are numbered* **I** *to* **VII**. *Numbers in parentheses correspond to amino acids not represented.* **Arrow** *after domain VII indicates amino acid whose charge varies depending on how the receptor is coupled with second messenger systems.* Data from Refs 6, 9–11, 19, 20.

The patent specification (at Example 1, page 8, line 30 et seq.) shows that, beginning with sequences that were derived from the third and sixth transmembrane domains of previously known G protein-linked receptors, the present inventors cloned and expressed a rat cDNA that encoded a novel serotonin receptor called St-B17 with high affinity for tricyclic psychotropic drugs. The pat spec (at page 12, line 15 et seq.) additionally shows that hydropathy analysis of the deduced amino acid sequence indicated seven hydrophobic regions predicted to represent putative transmembrane domains I-VII. The pat spec (at page 12, line 22 et seq.) further shows that when compared with previously known G protein-coupled receptors, the transmembrane domains of St-B17 exhibited homologies of 41%, 40%, 39%, 38%, 37%, and 36% to 5-HT2, 5-HT1D, 5-HT1C, 5-HT1B, 5-HT1A, and 5-HT1E serotonin receptors, respectively.

As indicated in Kohen et al., supra, a frame shift error had occurred in the rat clone, but the error occurred in the long carboxyl terminus tail, well past the seven transmembrane domains. As shown in Exhibits 1 and 2, a frame shift error had occurred in the human clone, too, but the error occurred in the long carboxyl terminus tail, well past the seven transmembrane domains, also. Monsma et al., supra, Figure 1, and Ruat et al., supra, Figure 1 for rat, and Kohen et al., supra, Figures 1 and 2 for human, illustrate the seven transmembrane domains. Trends in Pharmacology, supra, shows that, at the time of the Oct 26, 1992 priority date of the present application, transmembrane domain III and VI were known to contain conserved amino acids that were presumed to interact with the ligand, serotonin. Consistent with this information and the pat spec (at page 8, lines 31-34), the invention is claimed by reference to crucial transmembrane domains III and VI, the sequence from which was derived the degenerate primers to clone the rat cDNA encoding the novel serotonin receptor called St-B17.

VI. Monsma et al., Ruat et al., and Kohen et al.

As indicated above, the inventors cloned and expressed a novel serotonin receptor. There is no identity with other serotonin receptors as shown by the fact that the transmembrane domains of St-B17 exhibited homologies of 41%, 40%, 39%, 38%, 37%, and 36% to 5-HT2, 5-HT1D, 5-HT1C, 5-HT1B, 5-HT1A, and 5-HT1E serotonin receptors, respectively (see supra). Additionally, the above dates show that Monsma et al. and Ruat et al., describing the cloning of the rat St-B17 serotonin receptor, occurred at a time *after* the Oct 26, 1992 priority date of the present application in which the cloning of the rat St-B17 serotonin receptor is disclosed. Furthermore, the above dates show that Kohen et al., describing the cloning of the human St-B17 serotonin receptor, occurred at a time *after* the Oct 26, 1993 priority date of the present application in which the cloning of the human St-B17 serotonin receptor is disclosed. Because these scientific publications are not *prior* art, they cannot bar patentability of the present invention.

Conclusion

In view of the foregoing, Applicant respectfully requests that the present amendment be entered prior to examination of this application. It is respectfully submitted that the present application is in condition for allowance. Should any points remain that can be resolved by telephone, the Examiner is invited to contact the undersigned at the below-given telephone number.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 4/10/01

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Exhibit 1

12 = human
STB-17

Martinez/Needleman-Wunsch DNA Alignment
Minimum Match: 9; Gap Penalty: 1.10; Gap Length Penalty: 0.33

| Seq1(1>1984) | Seq2(1>1647) | Similarity | Gap | Gap | Consensus |
|---|---|---|---|---|---|
| h5-HT6 GSDB S40337 flatfile | Seq ID 12 h5-HT6 | Index | Number | Length | Length |
| (333>1984) | (1>1647) | 97.2 | 16 | 17 | 1658 |
| (333>1984) | (1>1647) | 97.2 | 16 | 17 | 1658 |

accession No for genbank

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          v340       v350       v360       v370       v380       v390       v400       v410
ACTCACCTCCCCCGGGGGGCGTGGTGAGTCGCGGTCTGTTCTCACGGACGGTCCCCGTCCAGCCTGCGCTTCGCCGGGGC
ACTCACCTCCCCCGGGGGGCGTGGTGAGTCGCGGTCTGTTCTCACG ACGGTCCCCGTCCAGCCTGCG TTCGCCGGGGC
ACTCACCTCCCCCGGGGGGCGTGGTGAGTCGCGGTCTGTTCTCACG-ACGGTCCCCGTCCAGCCTGCGGTTCGCCGGGGC
          ^10        ^20        ^30        ^40        ^50        ^60        ^70

          v420       v430       v440       v450       v460       v470       v480       v490
CCTCATCTGCTTTCCCGCCACCCTATCACTCCCTTGCCGTCCACCCTCGGTCCTCATGGTCCCAGAGCCGGGCCCAACCG
CCTCATCTGCTTTCCCGCCACCCTATCACTCCCTTGCCGTCCACCCTCGGTCCTCATGGTCCCAGAGCCGGGCCCAACCG
CCTCATCTGCTTTCCCGCCACCCTATCACTCCCTTGCCGTCCACCCTCGGTCCTCATGGTCCCAGAGCCGGGCCCAACCG
^80        ^90        ^100       ^110       ^120       ^130       ^140       ^150
                                                          start

          v500       v510       v520       v530       v540       v550       v560       v570
CCAATAGCACCCCGGCCTGGGGGGCAGGGCCGCC-GTCGGTCCCGGGGGGCAGCGGCTGGGTGGCGGCCGCG-CTGTGCG
CCAATAGCACCCCGGCCTGGGGGGCAGG C GCC GTCG     GGGGGGCAGCGGCTGGGTGGCGGCCG G CTGTGCG
CCAATAGCACCCCGGCCTGGGGGGCAGG-C-GCCCGTCGNNN--GGGGGGCAGCGGCTGGGTGGCGGCCG-GCCTGTGCG
^160       ^170       ^180       ^190       ^200       ^210       ^220       ^230

          v580       v590       v600       v610       v620       v630       v640       v650
TGGTCATCGCGCTGACGGCGGCGGCCAACTCGCTGCTGATCGCGCTCATCTGCACTCAGCCCGCGCTGCGCAACACGTCC
TGGTCATCGCGCTGACGGCGGCGGCCAACTCGCTGCTGATCGCGCTCATCTGCACTCAGCCCGCGCTGCGCAACACGTCC
TGGTCATCGCGCTGACGGCGGCGGCCAACTCGCTGCTGATCGCGCTCATCTGCACTCAGCCCGCGCTGCGCAACACGTCC
     ^240       ^250       ^260       ^270       ^280       ^290       ^300       ^310

          v660       v670       v680       v690       v700       v710       v720       v730
AACTTCTTCCTGGTGTCGCTCTTCACGTCTGACCTGATGGTGGGGCTGGTGGTGATGCCGCCGGCCATGCTGAACGCGCT
AACTTCTTCCTGGTGTCGCTCTTCACGTCTGACCTGATGGT GGGCTGGTGGTGATGCCGCCGGCCATGCTGAACGCGCT
AACTTCTTCCTGGTGTCGCTCTTCACGTCTGACCTGATGGTCGGGCTGGTGGTGATGCCGCCGGCCATGCTGAACGCGCT
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     ^320       ^330       ^340       ^350       ^360       ^370       ^380       ^390

          v740       v750       v760       v770       v780       v790       v800       v810
GTACGGGCGCTGGGTGCTGGCGCGCGGCCTCTGCCTGCTCTGGACCGCCTTCGACGTGATGTGCTGCAGCGCCTCCATCC
GTACGGGCGCTGGGTGCTGGCGCGCGGCCTCTGCCTGCTCTGGACCGCCTTCGACGTGATGTGCTGCAGCGCCTCCATCC
GTACGGGCGCTGGGTGCTGGCGCGCGGCCTCTGCCTGCTCTGGACCGCCTTCGACGTGATGTGCTGCAGCGCCTCCATCC
     ^400       ^410       ^420       ^430       ^440       ^450       ^460       ^470

          v820       v830       v840       v850       v860       v870       v880       v890
TCAACCTCTGCCTCATCAGCCTGGACCGCTACCTGCTCATCCTCTCGCCGCTGCGCTACAAGCTGCGCATGACGCCCCTG
TCAACCTCTGCCTCATCAGCCTGGACCGCTACCTGCTCATCCTCTCGCCGCTGCGCTACAAGCTGCGCATGACGCCCCTG
TCAACCTCTGCCTCATCAGCCTGGACCGCTACCTGCTCATCCTCTCGCCGCTGCGCTACAAGCTGCGCATGACGCCCCTG
     ^480       ^490       ^500       ^510       ^520       ^530       ^540       ^550

          v900       v910       v920       v930       v940       v950       v960       v970
CGTGCCCTGGCCCTAGTCCTGGGCGCCTGGAGCCTCGCCGCTCTCGCCTCCTTCCTGCCCCTGCTGCTGGGCTGGCACGA
CGTGCCCTGGCCCTAGTCCTGGGCG CTGGAGCCTCGCCGCTCTCGCCTCCTTCCTGCCCCTGCTGCTGGGCTGGCACGA
CGTGCCCTGGCCCTAGTCCTGGGCGGCTGGAGCCTCGCCGCTCTCGCCTCCTTCCTGCCCCTGCTGCTGGGCTGGCACGA
     ^560       ^570       ^580       ^590       ^600       ^610       ^620       ^630

          v980       v990       v1000      v1010      v1020      v1030      v1040      v1050
GCTGGGCCACGCACGGCCACCCGTCCCTGGCCAGTGCCGCCTGCTGGCCAGCCTGCCTTTTGTCCTTGTGGCGTCGGGCC
GCTGGGCCACGCACGGCCACCCGTCCCTGGCCAGTGCCGCCTGCTGGCCAGCCTGCCTTTTGTCCTTGTGGCGTCGGGCC
GCTGGGCCACGCACGGCCACCCGTCCCTGGCCAGTGCCGCCTGCTGGCCAGCCTGCCTTTTGTCCTTGTGGCGTCGGGCC
     ^640       ^650       ^660       ^670       ^680       ^690       ^700       ^710

          v1060      v1070      v1080      v1090      v1100      v1110      v1120      v1130
TCACCTTCTTCCTGCCCTCGGGTGCCATATGCTTCACCTACTGCAGGATCCTGCTAGCTGCCCGCAAGCAGGCCGTGCAG
TCACCTTCTTCCTGCCCTCGGGTGCCATATGCTTCACCTACTGCAGGATCCTGCTAGCTGCCCGCAAGCAGGCCGTGCAG
TCACCTTCTTCCTGCCCTCGGGTGCCATATGCTTCACCTACTGCAGGATCCTGCTAGCTGCCCGCAAGCAGGCCGTGCAG
     ^720       ^730       ^740       ^750       ^760       ^770       ^780       ^790

          v1140      v1150      v1160      v1170      v1180      v1190      v1200
GTGGCCTCCCTCACCACCGGCATGGCCAGTCAGGCCTCGGAGACGCTGCAGGTGCCCAGGACCCCACGCC-CAGGGGTGG
GTGGCCTCCCTCACCACCGGCATGGCCAGTCAGGCCTCGGAGACGCTGCAGGT CCCAGGA CCCA GC  CAGGGGTGG
GTGGCCTCCCTCACCACCGGCATGGCCAGTCAGGCCTCGGAGACGCTGCAGGTACCCAGGAGCCCA-GCGGCAGGGGTGG
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      ^800       ^810       ^820       ^830       ^840       ^850       ^860       ^870

v1210      v1220      v1230      v1240      v1250      v1260      v1270      v1280
AGTCTGCTGACAGCAGGCGTCTAGCCACGAAGCA-CAGCAGGAAGGCCCTGAAGGCCAGCCTGACGCTGGGCATCCTGCT
AGTCTGCTGACAGCAGGCGTCTAGC ACGAAG A CAGCAGGAAGG CCTGAAGGCCAGC TGACGCTGGGCATCCTGCT
AGTCTGCTGACAGCAGGCGTCTAGCAACGAAG-AGCAGCAGGAAGGGCCTGAAGGCCAGCATGACGCTGGGCATCCTGCT
      ^880       ^890       ^900       ^910       ^920       ^930       ^940       ^950

 v1290      v1300      v1310      v1320      v1330      v1340      v1350      v1360
GGGCATGTTCTTTGTGACCTGGTTGCCCTTCTTTGTGGCCAACATAGTCCAGGCCGTGTGCGACTGCATCTCCCCAGGCC
GGGCATGTTCTTTGTGACCTGGTTGCCCTTCTTTGTGGCCAACATAGTCCAGGCCGTGTGCGACTGCATCTCCCCAGGCC
GGGCATGTTCTTTGTGACCTGGTTGCCCTTCTTTGTGGCCAACATAGTCCAGGCCGTGTGCGACTGCATCTCCCCAGGCC
       ^960       ^970       ^980       ^990       ^1000      ^1010      ^1020      ^1030

 v1370      v1380      v1390      v1400      v1410      v1420      v1430      v1440
TCTTCGATGTCCTCACATGGCTGGGTTACTGTAACAGCACCATGAACCCCATCATCTACCCACTCTTCATGCGGACTTC
TCTTCGATGTCCTCACATGGCTGGGTTACTGTAACAGCACCATGAACCCCATCATCTACCCACTCTTCATGC GGACTTC
TCTTCGATGTCCTCACATGGCTGGGTTACTGTAACAGCACCATGAACCCCATCATCTACCCACTCTTCATGCTGGACTTC
       ^1040      ^1050      ^1060      ^1070      ^1080      ^1090      ^1100      ^1110

 v1450      v1460      v1470      v1480      v1490      v1500      v1510      v1520
AAGCGGGCGCTGGGCAGGTTCCTGCCATGTCCACGCTGTCCCCGGGAGCGCCAGGCCAGCCTGGCCTCGCCATCACTGCG
AAGCGGGCGCTGGGCAGGTTCCTGCCATGTCCACGCTGTCCCCGGGAGC CCAGGCCAGCCTGGCCTCGCCATCACTGCG
AAGCGGGCGCTGGGCAGGTTCCTGCCATGTCCACGCTGTCCCCGGGAGC-CCAGGCCAGCCTGGCCTCGCCATCACTGCG
       ^1120      ^1130      ^1140      ^1150      ^1160      ^1170      ^1180      ^1190

 v1530      v1540      v1550      v1560      v1570      v1580      v1590      v1600
CACCTCTCACAGCGGCCCCCGGCCCGGCCTTAGCCTACAGCAGGTGCTGCCGCTGCCCCTGCCGCCGGACTCAGATTCGG
CACCTCTCACAGCGGCCCCCGGCCCGGCCTTAGCCTACAGCAGGTGCTGCCGCTGCCCCTGCCGCCGGACTCAGATTCGG
CACCTCTCACAGCGGCCCCCGGCCCGGCCTTAGCCTACAGCAGGTGCTGCCGCTGCCCCTGCCGCCGGACTCAGATTCGG
       ^1200      ^1210      ^1220      ^1230      ^1240      ^1250      ^1260      ^1270

 v1610      v1620      v1630      v1640      v1650      v1660      v1670      v1680
ACTCAGACGCAGGCTCAGGCGGCTCCTCGGGCCTGCGGCTCACGGCCCAGCTGCTGCTTCCTGGCGAGGCCACCCAGGAC
ACTCAGACGCAGGCTCAGGCGGCTCCTCGGGC TGCGGCTCACGGCCCAGCTGCTGCTTCCTGGCGAGGCCACCCAGGAC
ACTCAGACGCAGGCTCAGGCGGCTCCTCGGGCGTGCGGCTCACGGCCCAGCTGCTGCTTCCTGGCGAGGCCACCCAGGAC
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        ^1280     ^1290     ^1300     ^1310     ^1320     ^1330     ^1340     ^1350

 v1690     v1700     v1710     v1720     v1730     v1740     v1750     v1760
CCCCCGCTGCCCACCAGGGCCGCTGCCGCCGTCAATTTCTTCAACATCG-ACCCCGCGGAGCCCGAGCTGCGGCCGCATC
CCCCCGCTGCCCACCAGGGCCGCTGCCGCCGTCAATTTCTTCAACATCG ACCCCGCGGAGCCCGAGCTGCGGCCGCATC
CCCCCGCTGCCCACCAGGGCCGCTGCCGCCGTCAATTTCTTCAACATCGSACCCCGCGGAGCCCGAGCTGCGGCCGCATC
        ^1360     ^1370     ^1380     ^1390     ^1400     ^1410     ^1420     ^1430

  v1770     v1780     v1790     v1800     v1810     v1820     v1830     v1840
CACTTGGCATCCCCACGAACTGACCCGGGCTTGGGGCTGGCCAATGGGGAGCTGGATTGAGCAGAACCCAGACCCTGAGT
CACTTGGCATCCCCACGAACTGACCC GGCTTGGGGCTGGCCAATGGGGAGCTGGATTGAGCAGAACCCAGACCCTGAGT
CACTTGGCATCCCCACGAACTGACCC-GGCTTGGGGCTGGCCAATGGGGAGCTGGATTGAGCAGAACCCAGACCCTGAGT
        ^1440     ^1450     ^1460     ^1470     ^1480     ^1490     ^1500     ^1510

  v1850     v1860     v1870     v1880     v1890     v1900     v1910     v1920
CCTTGGGCCAGCTCTTGGCTAAGACCAGGAGGCTGCAAGTCTCCTAGAAGCCCTCTGAGCTCCAGAGGGGTGCG-CAGAG
CCTTGGGCCAGCTCTTGGCTAAGACCAGGAGGCTGCAAGTCTCCTAGAAGCCCTCTGAGCTCCAGAGGGGTGCG CAGAG
CCTTGGGCCAGCTCTTGGCTAAGACCAGGAGGCTGCAAGTCTCCTAGAAGCCCTCTGAGCTCCAGAGGGGTGCGGCAGAG
        ^1520     ^1530     ^1540     ^1550     ^1560     ^1570     ^1580     ^1590

   v1930     v1940     v1950     v1960     v1970     v1980
CTGACCCCCTGCTGCCATCTCCAGGCCCCTTACCTGCAGGGATCATAGCTGACTCAGA
CTGACCCCCTGCTGCCATCTCCAGGCCCCTTACCTGCAGGGATCATAGCTGACT AGA
CTGACCCCCTGCTGCCATCTCCAGGCCCCTTACCTGCAGGGATCATAGCTGACT-AGA
        ^1600     ^1610     ^1620     ^1630     ^1640
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13

Exhibit 2

Lipman-Pearson Protein Alignment

Seq1(1>440) pep h5-HT6 GSDB S40337 Flatfile PEP (1>440)
Seq2(1>439) Seq ID 13 - h 5-HT6 from application (1>439)

| Similarity Index | Gap Number | Gap Length | Consensus Length |
|---|---|---|---|
| 79.6 | 5 | 5 | 442 |

Corrected version

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          v10       v20       v30       v40       v50       v60       v70       v80       v90       v100      v110      v120
MVPEPGPTANSTPAWGAGPPSAPGGSGWVAAALCVVIALTAAANSLLIALICTQPALRNTSNFFLVSLFTSDLMVGLVVMPPAMLNALYGRWVLARGLCLLWTAFDVMCCSASILNLCLI
||||||||||||||||||:... ||||||||:|||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
MVPEPGPTANSTPAWGAGARXX-GGSGWVAAGLCVVIALTAAANSLLIALICTQPALRNTSNFFLVSLFTSDLMVGLVVMPPAMLNALYGRWVLARGLCLLWTAFDVMCCSASILNLCLI
          ^10       ^20       ^30       ^40       ^50       ^60       ^70       ^80       ^90       ^100      ^110

          v130      v140      v150      v160      v170      v180      v190      v200      v210      v220      v230      v240
SLDRYLLILSPLRYKLRMTPLRALALVLGAWSLAALASFLPLLLGWHELGHARPPVPGQCRLLASLPFVLVASGLTFFLPSGAICFTYCRILLAARKQAVQVASLTTGMASQASETLQVP
||||||||||||||||||||||||||:|||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
SLDRYLLILSPLRYKLRMTPLRALALVLGGWSLAALASFLPLLLGWHELGHARPPVPGQCRLLASLPFVLVASGLTFFLPSGAICFTYCRILLAARKQAVQVASLTTGMASQASETLQVP
^120      ^130      ^140      ^150      ^160      ^170      ^180      ^190      ^200      ^210      ^220      ^230

          v250      v260      v270      v280      v290      v300      v310      v320      v330      v340      v350      v360
RTPRPGVESADSRRLATKHSRKALKASLTLGILLLGMFFVTWLPFFVANIVQAVCDCISPGLFDVLTWLGYCNSTMNPIIYPLFMRDFKRALGRFLPCPRCPRERQASLASPSLRTSHSGP
|:| :|||||||||||||| |||:||||:|||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
RSPAAGVESADSRRLATKSSRKGLKASMTLGILLLGMFFVTWLPFFVANIVQAVCDCISPGLFDVLTWLGYCNSTMNPIIYPLFMLDFKRALGRFLPCPRCPREPRPAWPRHHCAPLTAAP
^240      ^250      ^260      ^270      ^280      ^290      ^300      ^310      ^320      ^330      ^340      ^350

          v370      v380      v390      v400      v410      v420      v430      v440
RPGLSLQQVLPLP-LPPDSDSDSDAGSCG-SSGLRLTAQLLLPGEATQDPPLPTRAAAAVNFFNIDPAEPELRPHPLGIPTN
 |:|:  :  . |  ..:  ::::| ::  :.| | :  :| .   |.  | |.. :::::  . .||||||||||||||||
GPALAYSRCCRCPCRRTQIRTQTQAQAAPRACGSRPSCCFLARPPRTPPCP-PGPLPPSIGS-TSXPAEPELRPHPLGIPTN
^360      ^370      ^380      ^390      ^400      ^410      ^420      ^430
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